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Improvement of dimenhydrinate solubility by complexation with β-cyclodextrin

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Dimenhydrinate (DMH) is slightly soluble drug which belongs to class II of Biopharmaceutics classification system (low solubility, high permeability). To improve DMH solubility and enhance its bioavailability inclusion complexes with cyclodextrins (CDs) can be formed. These cyclic oligosaccharides with a hydrophilic outer surface incorporate a drug in the lipophilic central cavity and increase its solubility.

Phase solubility studies, where the change of drug solubility is corresponding to CD concentration, can be conducted to assess the binding characteristics of DMH and β-cyclodextrin (β-CD) and to determine the values of stability constant (K_s), complexation efficacy (CE) and utility number (U_{CD}). A-type phase solubility isotherms are characteristic for water soluble complexes. Optimal value of K_S is 100-5000 M^{-1}. Lower values imply very labile complexes with premature drug release and insignificant solubility improvement. Higher values imply very stable complexes with incomplete or obstructed drug release from CD cavity. The value of CE depends only on the slope of phase-solubility profile and it's is less variable compared to K_S value which depends on the intercept and intrinsic solubility which are affected by excipients used in formulation.

The results of the conducted phase solubility studies showed A_L-type isotherm. The slope was less than unity which implies that β-CD enhances the solubility of DMH linearly and forms 1:1 complex. The value of K_s was 171,10 M^{-1} and the CE value was 3,45. U_{CD} value ≥ 1 was achieved in 1,8% solution of β-CD thus solubilization of 25 mg of DMH was adequately provided by complexation with β-CD.